

Attorney Docket No.: **GCI-0017**
Inventors: **Wunderink et al.**
Serial No.: **09/973,850**
Filing Date: **October 10, 2001**
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In the Specification:

Please replace the paragraph at page 1, beginning at line 6, with the following:

This invention relates to diagnostic methods based upon a particular genotype in the Tumor Necrosis Factor (TNF α) gene, more specifically, a guanine (G) to adenine (A) transition at the -308 site in one of the TNF α genes (SEQ ID NO:1) giving a GA (SEQ ID NO:2) (or adenine adenine genotype, AA (SEQ ID NO:3)) genotype rather than the GG genotype (SEQ ID NO:1) at this locus. More specifically, this invention relates to a method for diagnosis of increased risk of death in patients with community-acquired pneumonia (CAP) and diagnosing pre-disposition or susceptibility to increased risk of death in patients who develop CAP, by screening for the presence of this A allele risk polymorphism. The invention also relates to compositions for screening for the polymorphism and improved treatment choices for patients having the polymorphism of the present invention. The invention also relates to screening assays and therapeutic and prophylactic methods.

Please replace the paragraph at page 5, line 31, through page 6, line 9, as follows:

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In a first aspect, the invention provides a method of diagnosing a disease condition associated with the A allele (GA (SEO ID NO:2) or AA (SEO ID NO:3) genotype) at the -308 site of TNF α (SEO ID NO:1). The first aspect of the invention further provides a method of identifying an animal, including a human, predisposed or susceptible to a risk associated with a particular genotype in a TNF α gene, said method comprising determining the genotype of said TNF α gene in said animal. In an embodiment of the invention, the method is to screen for an individual at risk of a condition or disease such as increased risk of death for patients with CAP by identifying the A allele (GA (SEO ID NO:2) or AA (SEO ID NO:3) genotype) in TNF α (SEO ID NO:1) at -308.

Please replace the paragraph at page 5, line 10 through 21 with the following:

The invention is based upon the observation reported herein of a correlation between the A allele (GA (SEO ID NO:2) or AA (SEO ID NO:3) genotype) in the TNF α gene (SEO ID NO:1), specifically at position -308, and an increased risk of death in patients with CAP. The invention is of advantage in that by screening for the presence of the polymorphism it is possible to identify individuals likely to have a genetic predisposition or susceptibility to such increased risk. It may also result in

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substantially different management, especially prevention and treatment (vaccination), if CAP occurs, with subsequent substantial improvement in mortality and morbidity from CAP in this especially at risk population.